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Description

The present invention relates to wound dressing materials.

When the skin is damaged by wounds including cuts and burns, various man-made dressing materials are used to heal the wounds.

The wound dressing materials are made of such synthetic materials as silicone compounds, nylon fabrics, or petrolatum gauzes and the like. These conventional wound dressing materials are inexpensive and easily available, however, they have poor affinity with the wounded area, and unsatisfactory from the point of view of promoting healing.

In order to obtain high-performance wound dressing materials, it is necessary to use natural materials of the properties similar to those of the patients' skin. To this end, heretofore, there have been provided lyophilized hog skins and non-woven fabric made of fibrous atelocollagen produced by alkali-treatment of the corium collagen of cattles. These conventional wound dressings are, however, still lacking in vapour permeability and antibacterial properties. In addition, it is difficult to assure uniform quality of manufacture of the conventional wound dressings, which makes the price of these conventional wound dressing materials high, and therefore, use of the materials is limited.

As for a combination of synthetic materials and natural materials to be used in wound dressings, Japanese Patent Publication No. 47470/1988 discloses a film produced from keration through solubilization of the keratin and graft-copolymerization of the thus solubilized keration with water-soluble polymers. Such a film is similar in composition to an organism or patients' skin, but due to deformation in the chemical structure, it cannot be expected that the film can provide the same properties as those of natural products.

According to one aspect of the present invention a wound dressing material is provided, made of animal-fibered fabric and produceable by a process wherein keratin layers of the surfaces of the animal fibers are stripped off to expose the non-keratin protein in the underlayers, whereby the surfaces of the animal fibers are modified to by hydrophillic, wherein said process comprises placing said animal fibers in an aqueous solution comprising water and an electrophiiic reagent, applying a mechanical strain essentially consisting of rapid bending and stretching to said animal fibers, and applying an oxidizing agent to said animal fibers in an amount effective to remove said keratin layers.

Such a wound dressing material can be produced to having excellent vapour permeability and antibacterial properties as in the case of the natural materials, and can be produced at relatively low cost and with an assured uniform quality.

In the wound dressing material of the present invention, it is preferable to use wool as the animal fibers, because wool is easily available and its processing techniques are well established.

The invention also includes a method of treating animal fibers to be used in producing a wound dressing material. There is already known from EP-A-0 055 778 and EP-A-0 019 639 a method for stripping off the keratin layers from the surfaces of the animal fibers but in accordance with the method of the present invention, prior to applying said oxidizing agent, the fibers are subjected to mechanical strain essentially consisting of rapid bending and stretching.

A preferred material is wool and the method may thus comprise the steps of imparting a mechanical strain such as that caused by rapid bending and stretching to the wool in a water bath containing a small amount of an electrophilic reagent such as Lewis acids so as to swell chemically active non-keratin protein existing in the vicinity of the surface layer of wool selectively, thereafter applying the Lewis acids to the swelled non-keratin protein of the wool so that the protein of the wool may lose its activity and the protein may serve as a temporary barrier, and then, under acidic conditions, applying an oxidizing agent to the surface of the wool to have the keratin layers in the surface layers of the wool rapidly stripped off therefrom and, at the same time, removing the Lewis acids applied to the wool therefrom through oxidation performed under the acidic conditions the oxidation reaction then being interrupted and the wool washed.

The above treatment may be carried out on the wool before it is woven, and the wool may be woven into fabric after the treatment. However, it is generally preferable to perform the treatment to wool already woven into a fabric.

In order to heal a damaged part of an organism or a patient, heretofore, similar part of an animal corresponding to the damaged part of the patient has been used. Thus, as for a wounded skin of the patient, it is in accordance with the same idea as the above to use the wound dressing materials made of the skins of mammals for healing.

On the other hand, typical matter for protecting bare skin of animals is pelage or animal's fibers, which is called "a second skin". The present invention was made on this basis.

However, each of the animal fibers has its outer peripheral surface covered with keratin which is a scleroprotein, and, when the animal fibers as obtained are woven or knitted into fabrics, such fabrics are not

adequate for a material for dressing the wound. This is due to the fact that corneums or horny tissues of the animal fibers repel water to make the animal fibers hydrophobic, and that the animal fibers are poor in affinity with the wounded area. It has been found that, even when keration fibers are solubilized by using hydrogen-bonding destroying agents and reducing agents and formed into a film, it is impossible for the film to sufficiently function of healing the wound because such a film has its native chemical structure deformed.

In view of these facts, the inventors of the present invention expected that, when the keratin layers are stripped off from the surfaces of the animal fibers to expose their hydrophilic layers, these hydrophilic layers may show much affinity with the wounded area, and carried out several experiments. Having obtained good experimental results, the inventors established the present invention.

EXAMPLE

A piece of moslin woolen fabric (specified in JIS-0803-1980, having a size of I/52 x 68/I and a weight of 102 + 5 g) was immersed in a bath of an solution of hydrochloric acid saturated with purified salt, and then subjecjed to a mechanical bending-and-stretching treatment for a period of from 2 to 3 minutes in the bath. After that, the treated piece of woolen fabric was dehydrated, and then immersed in a bath of an aqueous solution of hypochlorous acid (containing 4 % o.w.f. active chlorine) while subjected to further mechanical treatments similar to the above, whereby keratin layers existing in the surfaces of the wool were stripped off.

The piece of the treated fabric was then immersed in an acidic sodium sulfite solution to stop the oxidation, and washed repeatedly, and thereafter dried. The dried piece of woolen fabric was thoroughly washed in physiological saline.

In the above process, in place of the solution of hydrochloric acid saturated with the purified salt, it is possible to use a very dilute solution (20 to 50 ppm) of electrophilic reagents such as chlorides or acetates of cobalt (Co) and nickel (Ni). In this case it is necessary to add the step of treating the piece of woolen fabric in another bath containing inorganic acid at a low concentration after treating in the above oxidation-stopping bath, so as to renove the above metals from the piece of woolen fabric.

The wound dressing material of the present invention prepared as above was tested to determine the affinity with an organism in the following manner:

In the following test, seventy rats (Jbc-Wister rat) each of which was a 90 day old were used as laboratory animals. These rats were divided into the following four groups, depending on the test materials.

(Group 1)

for testing the moslin woolen fabric (hereinafter referred to simply as the "woolen fabric") which is a starting material of the wound dressing material of the present invention;

(Group 2)

for testing the wound dressing material of the present invention (hereinafter referred to as the "fabric of the invention);

(Group 3)

for testing a S-cyanoethylated keratin film (hereinafter referred to as the "keratin film") which was cast from. a formic acid solution; and

(Group 4)

for testing a sterilized and lyophilized hogskin corium (hereinafter referred to as the "hog skin") which is commercially available.

Each of the above Groups 1 to 4 contained fifteen rats, and was subdivided into three subgroups each of which contained five rats.

The entire body of each of the rats was anesthetized. Then, the rats received a round-shaped cut having a diameter of 2.0 cm) in its back median skin to form an incised skin wound.

On the other hand, round test pieces (having a diameter of 3.0 cm) of each of testing materials were cut out of the materials which were immersed in a sterilized physiological saline, and the skin wounds were

covered with the test pieces. At this the, a super glue or instant adhesive was applied to the back of the rat in its annular skin zone bordering the wound so as to prevent the test piece from falling off.

Healing effects of each of the test pieces on the wounds were observed with time through the naked eye. Some of the rats were killed after 3 and 7 days to obtain tissue samples of the wounds. The obtained tissue samples were fixed with formalin, and then embedded in paraffin, and the samples were then cut into microsections, each of which had a thickness of 6 microns. Each of the microsections was stained to facilitate the microscopic observation. In the naked eye observation, surface condition, amount of exudate and scab formation of each of the wounds were observed. Contraction rates in area of each of the wounds were determined by measuring an area of each of the wounds at intervals of predetermined period of days. Also, the adhesive properties of each of the test pieces and a period of time required for complete remedy. The complete remedy means a condition in which the lost skin was completely regenerated to close the wound completely, and the scab formed on the wounds completely fell off.

(Results of the Naked Eye Observation)

The wounds varied in appearance and internal condition with time, giving the data as shown in Table 1. Findings of the tissues are shown in Table 2.

Table 1

Test Group	Day of observation	Exudate Storage	Scab Formation	Contr'n of Wounds	Contr'n ate %
1	3rd day	+	unclear	-	0.1
	1 week	+	unclear	+	
2	3rd day	+	+	+	21.0
	1 week	-	+	+	
3	3rd day	++	-	-	8.2
	1 week	+	++	++	
4	3rd day	+	-	+	17.5
	1 week	+	-	+	

-: non +: small +: normal ++: large

Table 2

Test Group	Decomposition of Materials	Amount of Exudate	Blastema Formation	Epithelian Regeneration
1	good	large	poor	poor
2	better	small	good	good
3	bad	largest	bad	poor
4	poor	large	poor	good

Group 1 (woolen fabrics)

In the naked eye observation, the contraction of the wounds was poor on both the third and the seventh day, and the period required for complete regeneration of the lost skin of the wounds was long. This is probably due to the fact that the woolen fabrics of the test piece cannot sufficiently absorb the exudate issued from the wounds in the initial stage and that the woolen fabrics of the test piece stick to the wounds.

Based on the observation of the tissues of the wounds, it was found on the third day that there was a large storage of the exudate under the test piece, the exudate being issued from inflammatory tissues; and that the epithelial regeneration was poor. On the seventh day, it was clearly observed that fibers of the test piece were separated from each other, that neutrophils were deposited on these fibers, that decomposition absorption of these fibers of the test piece was promoted, and that purulent nidi and hemorrhagic nidi existed so as to prevent the blastema formation (i.e., fibrosing) from being promoted.

Group 2 (fabric of the invention)

Contraction of the wound was clearly observed on the third day. This is probably due to the fact that the fabric of the invention is excellent in properties of absorbing and drying the exudate tissues and sufficiently absorbed the exudate from the wound of the initial stage. It was also observed that a thin scab was formed over a large area of the wound under the test piece to promote regeneration of the epithelium or skin.

Based on the observation of the tissues, it was found that the decomposition absorption of the fibers of the test piece was most promoted, and regeneration of the epithelium was also promoted. Although normal congestion and bleeding were observed at the earlier stages, it was found on the seventh day and later that the blastema formation (i.e., fibrosing) was promoted under the scab, and a plenty of finer blood vessels were newly generated. further, regeneration of the epithelium (i.e., skin) over the entire area of the wound was found good.

Group 3 (keration film)

Although the contraction rate in area of the wound was still small on the third day, but way remarkably improved on the seventh day. The reason is considered to be that, since the keratin film of the test piece is poor in moisture-absorbtion and is irritative, a large storage of the exudate appears in a relatively earlier stage of the wound, and, since the keration film tends to be harder and too brittle, the test piece of the keration film covering the wound is broken at a relatively earlier stage of the wound to enhance the contraction of the wound drastically.

Based on the observation of the wounded tissues, no decomposition absorption of the test piece was found, and the test piece stuck to the entire surface of the wound. Probably due to the above, a large storage of the exudate was found. Even on the seventh day, the blastema formation (i.e., fibrosing) in the wounded tissues was still poor such as was found in case of the woolen fabric, and the congestion and bleeding remarkably occurred while an amount of the exudate still increased.

Group 4 (hog skin)

Contraction of the wound was found to be favorably promoted. Although the scab forced on the wound was thick and hard, it was supposed that the healing under the scab was smoothly promoted.

Based on the observation of the wounded tissues, it was found that, though no absorption of the hog skin was observed, there were produced a plenty of hair cracks and roughed areas in the test piece, through which it was supposed that the hog skin was being gradually decomposed. In the central area of the wound, it was found that the amount of initial bleeding was large, the amount of the exudate observed on the seventh day and later was also large, the blastema formation (i.e., fibrosing) in the wounded tissues was poor, but that the regeneration of the epithelium in the area bordering the wound tissues was remarkably promoted.

The wound dressing material of the present invention provides healing and regenerating effects on the patient's wound, the effects being superior to those of the conventional hog skin heretofore widely used by clinicians in hospitals.

The starting material of the wound dressing material of the present invention is wool fibers, which are easily available, and enables the user to select the in respect of length and fineness of the fiber, fineness and twist of the yarn and strand, suitable weaving and knitting type, and fabric density, whereby it is possible to produce the products having desirable properties such as contraction/expansion properties. In addition, the steps of the above processing can be easily carried out by using the conventional techniques widely used in the textile industry. Therefore, it is possible to provide the wound dressing material of the present invention at a low cost, which is equivalent to one several tenths of the cost of the conventional material made of the hog skin.

Claims

1. A wound dressing material made of animal-fibered fabric, produceable by a process wherein keratin layers of the surfaces of the animal fibers are stripped off to expose the non-keratin protein in the underlayers, whereby the surfaces of the animal fibers are modified to be hydrophillic, wherein said process comprises:
   (i) placing said animal fibers in an aqueous solution comprising water and an electrophilic reagent,
   (ii) applying a mechanical strain essentially consisting of rapid bending and stretching to said animal fibers,
   (iii) applying an oxidizing agent to said animal fibers in an amount effective to remove said keratin layers.

2. A wound dressing material according to claim 1 wherein wool provides the animal fibers of the fabric.

3. A method of producing a wound dressing material made of animal-fibered fabric, wherein keratin layers of the surfaces of the animal fibers are stripped off to expose the non-keratin protein in the underlayers, whereby the surfaces of the animal fibers are modified to be hydrophillic, said method comprising the steps of placing said animal fibers in an aqueous solution comprising water and an electrophilic reagent, and thereafter applying an oxidizing agent to said animal fibers in an amount effective to remove said keratin layers
   characterised in that
   prior to applying said oxidizing agent, the fibers are subjected to mechanical strain essentially consisting of rapid bending and stretching.

4. A method according to claim 3 in which wool is used as the animal fibers of the fabric.

5. A method of treating animal fibers to be used in producing a wound dressing material, wherein keratin layers of the surfaces of the animal fibers are stripped off to expose the non-keratin protein in the underlayers, whereby the surfaces of the animal fibers are modified to be hydrophillic, said method comprising the steps of placing said animal fibers in an aqueous solution comprising water and an electrophilic reagent, and thereafter applying an oxidizing agent to said animal fibers in an amount effective to remove said keratin layers
   characterised in that
   prior to applying said oxidizing agent, the fibers are subjected to mechanical strain essentially consisting of rapid bending and stretching.

6. Use of animal-fibered material in a wound dressing, said material having been treated to render the fiber surfaces hydrophillic by stripping of keratin layers from the surfaces of the fibers to expose the non-keratin protein of the layers while subjecting the fibers to mechanical treatment consisting essentially of rapid bending and stretching.

7. Use of a woolen material as a wound dressing according to claim 6.

Patentansprüche

1. Wundverbandmaterial aus einem Gewebe aus tierischen Fasern, das nach einem Verfahren hergestellt werden kann, worin Keratin-Schichten der Oberflächen der tierischen Fasern abgestreift werden, um das Nicht-Keratin-Protein in den unteren Schichten freizulegen, wodurch die Oberflächen der tierischen Fasern modifiziert werden, um hydrophil zu sein, worin das Verfahren umfaßt:
   (i) das Einbringen der tierischen Fasern in eine wäßrige Lösung aus Wasser und einem elektrophilen Reagens,
   (ii) das Aussetzen der tierischen Fasern einer mechanischen Belastung, die im wesentlichen aus raschem Biegen und Strecken besteht, und
   (iii) das Aufbringen eines Oxidationsmittels auf die tierischen Fasern in einer zur Entfernung der Keratin-Schichten wirksamen Menge.

2. Wundverbandmaterial nach Anspruch 1, worin die tierischen Fasern des Gewebes aus Wolle sind.

3. Verfahren zur Herstellung eines Wundverbandmaterials aus einem Gewebe aus tierischen Fasern, worin Keratin-Schichten der Oberflächen der tierischen Fasern abgestreift werden, um das Nicht-Keratin-Protein in den unteren Schichten freizulegen, wodurch die Oberflächen der tierischen Fasern modifiziert werden, um hydrophil zu sein, worin das Verfahren die Schritte des Einbringens der tierischen Fasern in eine wäßrige Lösung aus Wasser und einem elektrophilen Reagens und des anschließenden Aufbringens eines Oxidationsmittels auf die tierischen Fasern in einer zur Entfernung der Keratin-Schichten wirksamen Menge umfaßt,
   dadurch gekennzeichnet, daß vor dem Aufbringen des Oxidationsmittels die Fasern einer mechanischen Belastung ausgesetzt werden, die im wesentlichen aus raschem Biegen und Strecken besteht.

4. Verfahren nach Anspruch 3, worin für die tierischen Fasern des Gewebes Wolle verwendet wird.

5. Verfahren zur Behandlung von tierischen Fasern zur Verwendung bei der Herstellung eines Wundverbandmaterials, worin Keratin-Schichten der Oberflächen der tierischen Fasern abgestreift werden, um das Nicht-Keratin-Protein in den unteren Schichten freizulegen, wodurch die Oberflächen der tierischen Fasern modifiziert werden, um hydrophil zu sein, worin das Verfahren die Schritte des Einbringens der tierischen Fasern in eine wäßrige Lösung aus Wasser und einem elektrophilen Reagens und des anschließenden Aufbringens eines Oxidationsmittels auf die tierischen Fasern in einer zur Entfernung der Keratin-Schichten wirksamen Menge umfaßt, dadurch gekennzeichnet, daß vor dem Aufbringen des Oxidationsmittels die Fasern einer mechanischen Belastung ausgesetzt werden, die im wesentlichen aus raschem Biegen und Strecken besteht.

6. Verwendung eines Materials aus tierischen Fasern in einem Wundverband, wobei das Material behandelt wurde, um die Faseroberflächen hydrophil zu machen, indem Keratin-Schichten von den Oberflächen der Fasern abgestreift werden, um das Nicht-Keratin-Protein der Schichten freizulegen, während die Fasern einer mechanischen Behandlung ausgesetzt werden, die im wesentlichen aus raschem Biegen und Strecken besteht.

7. Verwendung eines Wollmaterials als Wundverband nach Anspruch 6.

Revendications

1. Matériau pour panser les blessures constitué de tissus à fibres animales, que l'on peut produire par un procédé où les couches de kératine des surfaces des fibres animales sont écaillées pour exposer la protéine non-kératine dans les sous-couches, grâce à quoi les surfaces des fibres animales sont modifiées pour être hydrophiles, où ledit procédé comprend :

(i) la mise en place desdites fibres animales dans une solution aqueuse contenant de l'eau et un réactif électrophile,
(ii) l'application d'une contrainte mécanique consistant essentiellement en une flexion et un étirement rapides auxdites fibres animales,
(iii) l'application d'un agent oxydant auxdites fibres animales en une quantité efficace pour éliminer lesdites couches de kératine.

2. Matériau pour panser les blessures selon la revendication 1 dans lequel la laine fournit les fibres animales du tissu.

3. Méthode de production d'un matériau pour panser les blessures constitué de tissus à fibres animales, dans laquelle les couches de kératine des surfaces des fibres animales sont écaillées pour exposer la protéine non-kératine dans les sous-couches, grâce à quoi les surfaces des fibres animales sont modifiées pour être hydrophiles, ladite méthode comprenant les étapes de mise en place desdites fibres animales dans une solution aqueuse comprenant de l'eau et un réactif électrophile, et après cela l'application d'un agent oxydant auxdites fibres animales en une quantité efficace pour éliminer lesdites couches de kératine

caractérisée en ce que avant l'application dudit agent oxydant, les fibres sont soumises à une contrainte mécanique consistant essentiellement en une flexion et un étirement rapides.

4. Méthode selon la revendication 3 dans laquelle de la laine est utilisée en tant que fibres animales du tissu.

5. Méthode de traitement de fibres animales à utiliser dans la production d'un matériau pour panser les blessures, dans laquelle les couches de kératine des surfaces des fibres animales sont écaillées pour exposer la protéine non-kératine dans les sous-couches, grâce à quoi les surfaces des fibres animales sont modifiées pour être hydrophiles, ladite méthode comprenant les étapes de mise en place desdites fibres animales dans une solution aqueuse comprenant de l'eau et un réactif électrophile, et après cela l'application d'un agent oxydant auxdites fibres animales en une quantité efficace pour éliminer lesdites couches de kératine

caractérisée en ce que avant l'application dudit agent oxydant, les fibres sont soumises à une contrainte mécanique consis tant essentiellement en une flexion et un étirement rapides.

6. Utilisation d'un matériau à fibres animales dans un pansement de blessure, ledit matériau ayant été traité pour rendre les surfaces des fibres hydrophiles en écaillant les couches de kératine des surfaces des fibres pour exposer la protéine non-kératine des couches tout en soumettant les fibres à un traitement mécanique consistant essentiellement en une flexion et un étirement rapides.

7. Utilisation d'un matériau de laine comme pansement de blessure selon la revendication 6.